SEQ ID No. 15, SEQ ID No. 17 or SEQ ID No. 20, homologs thereof and functional fragments thereof.

REMARKS

The present amendment is being filed in order to amend the specification in accordance with the floppy disk with the sequences filed herewith. The floppy disk was not generated in the same way the sequences were generated at the time of filing the PCT application. For the genes encoding the protein, the PCT provides the "subsequences". Therefore, a shift had to occur and the diskette filed herewith contains the sequences generated using the proper software. The following table gives the correspondence between the sequences and the specification and claims have been amended accordingly.

| SEQ ID No. in PCT Publication | SEQ No. in Electronic Sequence Listings | SEQ ID No. in PCT Publication | SEQ No. in Electronic Sequence Listings |
|---|---|---|---|
| 1 | 1 | 10 | 15 |
| 2 | 2 | 11 | 17 |
| 3 | 4 | 12 | 19 |
| 4 | 5 | 13 | 20 |
| 5 | 7 | 14 | 22 |
| 6 | 8 | 15 | 23 |
| 7 | 10 | 16 | 24 |
| 8 | 12 | 17 | 25 |
| 9 | 13 | | |

Applicants are submitting herewith a hard copy of the sequence listing as well as the computer readable form (CRF) of the sequence listing. The contents of the paper sequence listing and the computer readable form are the same and where applicable, include no new matter as required by 37 CFR 1.821(e). 1.821(f), 1.821(g), 1.825(b) or 1.825(d).

Respectfully submitted,
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CAM:ds
Enclosures

According to another embodiment of the method of the invention said functional similar genes are essential genes from Candida Spp., preferably Candida albicans, or from Aspergillus Spp., preferably from Aspergillus fumigatus.

According to another aspect, the present invention concerns a polynucleotide having the sequence as depicted in SEQ ID No.2, SEQ ID No.5, SEQ ID No.8, SEQ ID No.10, SEQ ID No.13, SEQ ID No.15, SEQ ID No.17 or SEQ ID No.20, preferably SEQ ID No.2, SEQ ID No.5, SEQ ID No.8, SEQ ID No.13, SEQ ID No.15 or SEQ ID No.17, homologs thereof and functional fragments thereof.

According to another aspect, the present invention concerns a gene which is CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, preferably CaOR110, CaMR212, CaNL256, CaBR102 or CaIR012, or a functionally similar gene or a functional fragment thereof.

According to this embodiment, the functionally similar gene or homologous polynucleotide has a sequence identity, at the nucleotide level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, of at least 50%, preferably of at least 60%, and most preferably of at least 70%. A functional fragment is a polynucleotide fragment that will retain the functionality of the starting product (nucleotide or gene). One example is the CaOR110 splice variant (which is also homologous to the original gene, with about 90% identity).

According to another embodiment, the functionally similar gene has a sequence identity, at the amino-acid level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, encoded protein(s) of at least 40%, preferably of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

Example 2 : CaBR102

The Internet site of Stanford (http://candida.stanford.edu/) give access to preliminary sequences of the genome of C. albicans. One of these sequences has homology with the YBR102 gene of S.cerevisiae. Two oligonucleotides were selected in this sequence (5'-AGTATTCAATTGGGTATTCC-3' and 5'-CCGGCATCATCAGTAACTCC-3') in order to amplified the corresponding fragment of C. albicans. After cloning, we obtained a sequence of 647 bp (SEQ ID NO:4). The deduced protein was compared with the one of YNL102, evidencing 35% similarity and 26% identity (fig.2). This fragment was amplified using Pfu polymerase (Stratagene). The PCR product was purified (High Pure PCR Product Purification Kit, Boehringer Mannheim) and used as a probe for screening a C. albicans genomic DNA library. The latter was prepared by partial digestion of C. albicans genomic DNA with SauIIIA and cloning into the YEP-24TRP1 vector at the BamHI restriction site. 40,000 clones of the library were then spread at a density of 2000 clones per dish. Each dish was covered by a nitrocellulose filter (Membrane Hybond N$^+$, Amersham) which was then successively treated with : 1.5 M NaCl/0.5 M NaOH, 5 minutes; 1.5 M NaCl/0.5 M Tris-HCl pH 7.2/1 mM EDTA, 3 minutes, twice; DNA was crosslinked to the filters (Amersham Life Science, ultra violet crosslinker). The probe (100 ng) was labelled with $^{32}P$ using the RediPrime kit and dCTP (Amersham Life Science). The filters were hybridized in a buffer containing 30% formamide, 5 x SSC, 5% Denhart's solution, 1% SDS, 100 $\mu$g /ml salmon sperm DNA and a probe concentration of $10^6$ cpm/ml at 42°C for 16 h. The membranes were then washed three times at room temperature in 2 x SSC/0.1% SDS for 5 minutes each and three times in 1 x SSC/0.1% SDS at 60°C for 20 minutes each. the filters were then exposed overnight to an X-ray

film. The colonies corresponding to the positives clones were isolated and screened a second time by the same procedure. Two positives clones were finally obtained, which were sequenced on an ABI377 apparatus. the sequences were compiled using ABI software and then analysed using the GCG software package. The nucleotide sequences of these two clones were identical and contained the complete coding sequence corresponding to the probe used, this gene was called CaBR102, whose sequence is represented in SEQ ID No:4. The translation of this nucleotide sequence was examined, account was taken of the fact that in C. albicans the CTG codon is translated to serine (there are 3 CTG codons in CaBR102). The deduced protein has 24% identity to S. cerevisiae gene YBR102.

Example 3 : CaIR012

Chromosomal DNA from the C. albicans strain Caf2-1 was isolated using Yeast Cell Lysis prep Kit and Genome DNA Kit from BIO101. A 343 bp fragment from C. albicans genomic DNA (SEQ ID NO:7) was amplified with the oligonucleotide primers CaYIR012-5' (5'-GACGTCGTAGACGATACTCAAGAAG-3') and CaYIR012-3' (5'-CTGCAGTAAACCCTCCAGATATAACAG-3') by PowerScript DNA polymerase (PAN Systems GmbH) using the hot start technique. The PCR product was purified from the agarose gel and labeled with fluorescein (Gene image random prime labelling module, Amersham Life Science) according to the manufacturer's instructions. Plasmid DNA from E.coli was isolated using Qiagen columns as recommended by the manufacturer. Screening the λZAPII C. albicans cDNA library was performed following the manufacturer's instructions (Stratagene Ltd.). Nylon filters (Schleicher&Schuell) were lifted from LB-plates (150 mm) with 15000 pfu/plate, denatured 5 min in 1.5M NaCL, 0.5M NaOH, neutralized 3 min in 1.5M NaCl, 0.5M Tris-HCl pH8.0, washed 3 min in 0.2 M Tris-HCl pH 7.5, 2xSSC and DNA was

crosslinked to the filters (Stratagene UV crosslinker). The filters were prehybridized 4 h at 60 °C and hybridized with the fluorescein-labeled DNA probe overnight at 60 °C. Detection was performed with Anti-fluorescein AP conjugate (Signal amplification module for the FluorImager, Amersham LIFE SCIENCE) and analysed after 20 h with a Fluorimager (Storm 860, Molecular Dynamics). Positive plaques were picked and incubated with 0.5 ml SM-buffer (100mM NaCl, 8 mM $MgSO_4$, 50 mM Tris-HCl pH7.5, 0,01% gelatin). The selected clones were diluted, titered with host cells XL1-Blue and screened and purified a second time by the same procedure. Finally, the pBluescript SK(-) phagemid containing the DNA insert of interest was rescued by the ExAssist Helper Phage system according to the Stratagene protocol. From a total of 75000 screened plaques, 3 positive clones were identified. pBluescript SK (-) phagemid DNA was isolated, sequenced with T3 and T7 primers and the sequences were extended with custom-synthesized oligonucleotide primers. Nucleotide sequence analyses were performed with the Gene Data software package (Gene Data AG, Basel Switzerland). Similarity searches with the Swissprot database were conducted with the BLAST program (Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.). One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaIR1012, whose sequence is represented in SEQ ID NO:8.

Example 4: CaJL039

The CaJL039 sequence is depicted in SEQ ID No 7.

The CaJL039 gene was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A fragment that showed homology to *Saccharomyces cerevisiae* YJL039c was identified, the sequence of which is given in SEQ ID No 12.

Using the procedure disclosed in example 3 with the oligonucleotide primer pair (Ca039s: TAG CTC AAC CTA CCA CCA ATC /Ca039r: ATC ACA AGA CTG TCA ATG TAA AT), a short PCR fragment (234 base pairs long) was amplified for screening a Candida albicans cDNA lambda ZAP II library (gift of Alistair Brown, Aberdeen).

Three positive clones of the 3' coding region were obtained. (# 21t7, 11t3, 21t3).

(b) 3'- and 5'- extension of the internal fragment using the primer walking method

The Sanglard genomic Candida DNA library with the YEp24 vector backbone was used for further amplification of 3'- and 5'-coding sequences. Amplification was carried out by using the following vector-specific oligonucleotide primers and CaJL039 fragment-specific primers:

cggaattcctatcgactacgcgatcatgg: YEp24for (vector specific)

gcgaattccgatataggcgccagcaac: YEp24ba (vector specific)

caattgctttgactcgggtgttattaagt: Ca039-51 (CaJL039: 5'fishing)

tcttggcacaacttgataagaatctgt: Ca039-52 (`)

taggtgtacgcgaaagccaagtagaac:Ca039-53 (`)

ttgttaatcgtacacctaaggtgttgac: Ca039-31 (CaJL039: 3'fishing)

ttgcagattgatgctagcaatgtatttg: Ca039-32 (`)

Using the technique of primer walking, the complete 5'-sequence could be amplified (clone 14b-1-1 and clone 17b-3-4).

The missing 3'-sequence was available from GTC PathoGenome Release 5.0, contig #2830.

An interacting protein (C82, component for RNA polymerase III in yeast) has been identified.

Example 5: CaOR110

5.1. CaOR110

The CaOR110 sequence is depicted in SEQ ID No 13.

CaOR110 was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A small ScOR110-homologous fragment was used in a hybridization experiment to identify CaOR110 clones in a *Candida Albicans* lambda ZAPII cDNA library (from Alistair Brown). Alignement of Candida Albicans CaOR110 sequence with the fragment used for hybridization is given in figure 3. The homologous fragment sequence is given in SEQ ID No. 23.

(b) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This amplification was done by using the vector-specific oligos (directional towards the insert) and CaOR110 fragment-specific oligos (directional towards the vector flanking sequences) described below:

cggaattcctatcgactacgcgatcatgg : YEP24for

gcgaattccgatataggcgccagcaac : YEP24ba

cgggatccggtaaccaattggatctataaccgtg : 110-ba-150

gcggatcctggtgcccttggtggtgaatg : CaYOR110A

gcggatccctcacaatatgacgattgaaact : CaYOR110B

ggcgtcgactcaggcgccagttttacgtacttcaaattcatc : CaYOR110C

tgtgaattcttgacacagggtga : CaYOR110D

caaaccttcagcacaactcca : CaYOR110E

The finaly assembled sequence that included also 3´- and 5´- non-coding sequences was verified by sequencing. The coding region was subcloned into the p414RSGALL-vector.

The map is depicted in Fig. 4.

The homologous yeast ORF (YOR110w) has been described as the transcription factor subunit TFC7 interacting with TFC1 in the TFIIIC polymerase complex (Manaud et al., 1998, Mol. Cell. Biol. 18; 3191-3200).

5.2. CaOR110 splice variant

For CaOR110, an additional splice variant was identified. The clones for the splice variant of CaOR110 were obtained from a Candida albicans cDNA library.

The sequence is depicted in SEQ ID No. 15.

The splice variant uses the donor site "gtacgt" at position 907 of the original CaOR110 sequence. Acceptor site is at 1047. The map is disclosed in Fig. 5.

The alignement of the original CaOR110 and the splice variant is given in fig. 6.

Example 6 : CaMR212

The CaMR212 sequence is depicted in SEQ ID No. 17.

(a) CaMR212 was cloned based on gene fragment data from the public Standford *Candida albicans* sequencing database.

The sequence of a fragment showing homology (Blast search) to the *Saccharomyces cerevisiae* gene YMR212c is given in SEQ ID 16.

Based on these data, the following oligos were designed that allow amplification of this fragment (490 bp-fragment) from genomic *Candida albicans* DNA.

Oligos:

CaYMR212for: 5´- cacctgtgaacaacccaccatc-3´

CaYMR212back: 5´- gaatatccttttttaactcaagag -3´

(b) 3´- and 5´- extension of this internal fragment from CaMR212

For this purpose, genomic Candida DNA libraries from Dominique Sanglard (received from RMV) were used. The YEp24 backbone of this library was used to amplify the 3´- and 5´- coding and non coding sequences with PCR. This was done

by microscope analysis of YMR212-GFP fusion proteins and by biochemical analysis of YMR212-GST fusion proteins).

Example 7 : CaDR325

The CaDR325 sequence is given at SEQ ID 20.

CaDR325 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

(a) 3 fragments that showed homology to *Saccharomyces cerevisiae* YDR325 were identified, the sequences of which are disclosed in SEQ ID 22, 23 and 24.

Based on these data, the following oligos were designed that allowed the verification of the database sequences and the amplification of an approx. 2200 bp internal CaDR325 fragment from genomic DNA:

cgagcatctacttgttcaaccac: hybCaYDR325ba Oligo

gaatctctggctcgctc: 325-juls Oligo

gaccgagatacacgagaat: 325-julr Oligo

ggttaaatgatcgtgatgaat: Ca325r Oligo

caacctcactgacaaatactt: Ca325s Oligo

The finally subcloned 2200 bp internal fragment was amplified by the combination hybCaYDR325ba + 325-julr oligos.

(c) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This was done by using the following vector-specific oligos (directional towards the insert) and CaDR325 2200 bp fragment-specific oligos (directional towards the vector flanking sequences):

cggaattcctatcgactacgcgatcatgg : YEP24for (vector specific)

gcgaattccgatataggcgccagcaac : YEP24ba (vector specific)

acgcttccaatgtattattctcg : Oligo 1-10-A back

Example 2 : CaBR102

The Internet site of Stanford (http://candida.stanford.edu/) give access to preliminary sequences of the genome of C. albicans. One of these sequences has homology with the YBR102 gene of S.cerevisiae. Two oligonucleotides were selected in this sequence (5'-AGTATTCAATTGGGTATTCC-3' and 5'-CCGGCATCATCAGTAACTCC-3') in order to amplified the corresponding fragment of C. albicans. After cloning, we obtained a sequence of 647 bp (SEQ ID NO:4). The deduced protein was compared with the one of YNL102, evidencing 35% similarity and 26% identity (fig.2). This fragment was amplified using Pfu polymerase (Stratagene). The PCR product was purified (High Pure PCR Product Purification Kit, Boehringer Mannheim) and used as a probe for screening a C. albicans genomic DNA library. The latter was prepared by partial digestion of C. albicans genomic DNA with SauIIIA and cloning into the YEP-24TRP1 vector at the BamHI restriction site. 40,000 clones of the library were then spread at a density of 2000 clones per dish. Each dish was covered by a nitrocellulose filter (Membrane Hybond N+, Amersham) which was then successively treated with : 1.5 M NaCl/0.5 M NaOH, 5 minutes; 1.5 M NaCl/0.5 M Tris-HCl pH 7.2/1 mM EDTA, 3 minutes, twice; DNA was crosslinked to the filters (Amersham Life Science, ultra violet crosslinker). The probe (100 ng) was labelled with $^{32}P$ using the RediPrime kit and dCTP (Amersham Life Science). The filters were hybridized in a buffer containing 30% formamide, 5 x SSC, 5% Denhart's solution, 1% SDS, 100 µg /ml salmon sperm DNA and a probe concentration of $10^6$ cpm/ml at 42°C for 16 h. The membranes were then washed three times at room temperature in 2 x SSC/0.1% SDS for 5 minutes each and three times in 1 x SSC/0.1% SDS at 60°C for 20 minutes each. the filters were then exposed overnight to an X-ray

film. The colonies corresponding to the positives clones were isolated and screened a second time by the same procedure. Two positives clones were finally obtained, which were sequenced on an ABI377 apparatus. the sequences were compiled using ABI software and then analysed using the GCG software package. The nucleotide sequences of these two clones were identical and contained the complete coding sequence corresponding to the probe used, this gene was called CaBR102, whose sequence is represented in SEQ ID No:4. The translation of this nucleotide sequence was examined, account was taken of the fact that in C. albicans the CTG codon is translated to serine (there are 3 CTG codons in CaBR102). The deduced protein has 24% identity to S. cerevisiae gene YBR102.

Example 3 : CaIR012

Chromosomal DNA from the C. albicans strain Caf2-1 was isolated using Yeast Cell Lysis prep Kit and Genome DNA Kit from BIO101. A 343 bp fragment from C. albicans genomic DNA (SEQ ID NO:7) was amplified with the oligonucleotide primers CaYIR012-5' (5'-GACGTCGTAGACGATACTCAAGAAG-3') and CaYIR012-3' (5'-CTGCAGTAAACCCTCCAGATATAACAG-3') by PowerScript DNA polymerase (PAN Systems GmbH) using the hot start technique. The PCR product was purified from the agarose gel and labeled with fluorescein (Gene image random prime labelling module, Amersham Life Science) according to the manufacturer's instructions. Plasmid DNA from E.coli was isolated using Qiagen columns as recommended by the manufacturer. Screening the λZAPII C. albicans cDNA library was performed following the manufacturer's instructions (Stratagene Ltd.). Nylon filters (Schleicher&Schuell) were lifted from LB-plates (150 mm) with 15000 pfu/plate, denatured 5 min in 1.5M NaCL, 0.5M NaOH, neutralized 3 min in 1.5M NaCl, 0.5M Tris-HCl pH8.0, washed 3 min in 0.2 M Tris-HCl pH 7.5, 2xSSC and DNA was

crosslinked to the filters (Stratagene UV crosslinker). The filters were prehybridized 4 h at 60 °C and hybridized with the fluorescein-labeled DNA probe overnight at 60 °C. Detection was performed with Anti-fluorescein AP conjugate (Signal amplification module for the FluorImager, Amersham LIFE SCIENCE) and analysed after 20 h with a Fluorimager (Storm 860, Molecular Dynamics). Positive plaques were picked and incubated with 0.5 ml SM-buffer (100mM NaCl, 8 mM $MgSO_4$, 50 mM Tris-HCl pH7.5, 0,01% gelatin). The selected clones were diluted, titered with host cells XL1-Blue and screened and purified a second time by the same procedure. Finally, the pBluescript SK(-) phagemid containing the DNA insert of interest was rescued by the ExAssist Helper Phage system according to the Stratagene protocol. From a total of 75000 screened plaques, 3 positive clones were identified. pBluescript SK (-) phagemid DNA was isolated, sequenced with T3 and T7 primers and the sequences were extended with custom-synthesized oligonucleotide primers. Nucleotide sequence analyses were performed with the Gene Data software package (Gene Data AG, Basel Switzerland). Similarity searches with the Swissprot database were conducted with the BLAST program (Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.). One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaIR1012, whose sequence is represented in SEQ ID NO:8.

Example 4: CaJL039

The CaJL039 sequence is depicted in SEQ ID No 7.

The CaJL039 gene was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A fragment that showed homology to *Saccharomyces cerevisiae* YJL039c was identified, the sequence of which is given in SEQ ID No 12.

Using the procedure disclosed in example 3 with the oligonucleotide primer pair (Ca039s: TAG CTC AAC CTA CCA CCA ATC /Ca039r: ATC ACA AGA CTG TCA ATG TAA AT), a short PCR fragment (234 base pairs long) was amplified for screening a Candida albicans cDNA lambda ZAP II library (gift of Alistair Brown, Aberdeen).

Three positive clones of the 3' coding region were obtained. (# 21t7, 11t3, 21t3).

(b) 3'- and 5'- extension of the internal fragment using the primer walking method

The Sanglard genomic Candida DNA library with the YEp24 vector backbone was used for further amplification of 3'- and 5'-coding sequences. Amplification was carried out by using the following vector-specific oligonucleotide primers and CaJL039 fragment-specific primers:

cggaattcctatcgactacgcgatcatgg: YEp24for (vector specific)

gcgaattccgatataggcgccagcaac: YEp24ba (vector specific)

caattgctttgactcgggtgttattaagt: Ca039-51 (CaJL039: 5'fishing)

tcttggcacaacttgataagaatctgt: Ca039-52 (`)

taggtgtacgcgaaagccaagtagaac:Ca039-53 (`)

ttgttaatcgtacacctaaggtgttgac: Ca039-31 (CaJL039: 3'fishing)

ttgcagattgatgctagcaatgtatttg: Ca039-32 (`).

Using the technique of primer walking, the complete 5'-sequence could be amplified (clone 14b-1-1 and clone 17b-3-4).

The missing 3'-sequence was available from GTC PathoGenome Release 5.0, contig #2830.

An interacting protein (C82, component for RNA polymerase III in yeast) has been identified.

Example 5: CaOR110

5.1. CaOR110

The CaOR110 sequence is depicted in SEQ ID No 13.

CaOR110 was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A small ScOR110-homologous fragment was used in a hybridization experiment to identify CaOR110 clones in a *Candida Albicans* lambda ZAPII cDNA library (from Alistair Brown). Alignement of Candida Albicans CaOR110 sequence with the fragment used for hybridization is given in figure 3. The homologous fragment sequence is given in SEQ ID No. 25.

(b) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This amplification was done by using the vector-specific oligos (directional towards the insert) and CaOR110 fragment-specific oligos (directional towards the vector flanking sequences) described below:

cggaattcctatcgactacgcgatcatgg : YEP24for

gcgaattccgatataggcgccagcaac : YEP24ba

cgggatccggtaaccaattggatctataaccgtg : 110-ba-150

gcggatcctggtgcccttggtggtgaatg : CaYOR110A

gcggatccctcacaatatgacgattgaaact : CaYOR110B

ggcgtcgactcaggcgccagttttacgtacttcaaattcatc : CaYOR110C

tgtgaattcttgacacagggtga : CaYOR110D

caaaccttcagcacaactcca : CaYOR110E

The finaly assembled sequence that included also 3´- and 5´- non-coding sequences was verified by sequencing. The coding region was subcloned into the p414RSGALL-vector.

The map is depicted in Fig. 4.

The homologous yeast ORF (YOR110w) has been described as the transcription factor subunit TFC7 interacting with TFC1 in the TFIIIC polymerase complex (Manaud et al., 1998, Mol. Cell. Biol. 18; 3191-3200).

5.2. CaOR110 splice variant

For CaOR110, an additional splice variant was identified. The clones for the splice variant of CaOR110 were obtained from a Candida albicans cDNA library.

The sequence is depicted in SEQ ID No.15.

The splice variant uses the donor site "gtacgt" at position 907 of the original CaOR110 sequence. Acceptor site is at 1047. The map is disclosed in Fig. 5.

The alignement of the original CaOR110 and the splice variant is given in fig. 6.

Example 6 : CaMR212

The CaMR212 sequence is depicted in SEQ ID No.17.

(a) CaMR212 was cloned based on gene fragment data from the public Standford *Candida albicans* sequencing database.

The sequence of a fragment showing homology (Blast search) to the *Saccharomyces cerevisiae* gene YMR212c is given in SEQ ID 19.

Based on these data, the following oligos were designed that allow amplification of this fragment (490 bp-fragment) from genomic *Candida albicans* DNA.

Oligos:

CaYMR212for: 5´- cacctgtgaacaacccaccatc-3´

CaYMR212back: 5´- gaatatccttttttaactcaagag -3´

(b) 3´- and 5´- extension of this internal fragment from CaMR212

For this purpose, genomic Candida DNA libraries from Dominique Sanglard (received from RMV) were used. The YEp24 backbone of this library was used to amplify the 3´- and 5´- coding and non coding sequences with PCR. This was done

by microscope analysis of YMR212-GFP fusion proteins and by biochemical analysis of YMR212-GST fusion proteins).

Example 7 : CaDR325

The CaDR325 sequence is given at SEQ ID 20.

CaDR325 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

(a) 3 fragments that showed homology to *Saccharomyces cerevisiae* YDR325 were identified, the sequences of which are disclosed in SEQ ID 22, 23 and 24.

Based on these data, the following oligos were designed that allowed the verification of the database sequences and the amplification of an approx. 2200 bp internal CaDR325 fragment from genomic DNA:

cgagcatctacttgttcaaccac: hybCaYDR325ba Oligo

gaatctctggctcgctc: 325-juls Oligo

gaccgagatacacgagaat: 325-juir Oligo

ggttaaatgatcgtgatgaat: Ca325r Oligo

caacctcactgacaaatactt: Ca325s Oligo

The finally subcloned 2200 bp internal fragment was amplified by the combination hybCaYDR325ba + 325-julr oligos.

(c) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This was done by using the following vector-specific oligos (directional towards the insert) and CaDR325 2200 bp fragment-specific oligos (directional towards the vector flanking sequences):

cggaattcctatcgactacgcgatcatgg : YEP24for (vector specific)

gcgaattccgatataggcgccagcaac : YEP24ba (vector specific)

acgcttccaatgtattattctcg : Oligo 1-10-A back

MARKED UP VERSION OF CLAIMS

**Claims:**

1. A polynucleotide having the sequence as depicted in the sequence selected from the group consisting of SEQ ID No.2, SEQ ID No.~~4~~ 5, SEQ ID No.~~6~~ 8, SEQ ID No.~~7~~ 10, SEQ ID No.~~9~~ 8, SEQ ID No.~~10~~ 15, SEQ ID No.~~11~~ 17 or SEQ ID No.~~13~~ 20, homologs thereof and functional fragments thereof.

2.-The polynucleotide of claim 1 which is the gene CaNL256, homologs thereof and functional fragments thereof.

3.-The polynucleotide of claim 1 which is the gene CaBR102, homologs thereof and functional fragments thereof.

4.-The polynucleotide of claim 1 which is the gene CaIR012, homologs thereof and functional fragments thereof.

5.-The polynucleotide of claim 1 which is the gene CaMR212, homologs thereof and functional fragments thereof.

6.-The polynucleotide of claim 1 which is the gene CaDR325, homologs thereof and functional fragments thereof.

7.-The polynucleotide of claim 1 which is the gene CaOR110, homologs thereof and functional fragments thereof.

8.-The polynucleotide of claim 1 which is the gene CaJL039, homologs thereof and functional fragments thereof.

9 -A protein encoded by the polynucleotide according to claim 2 or a functional polypeptide fragment thereof.

10 -A protein encoded by the polynucleotide according to claim 3 or a functional polypeptide fragment thereof.